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EXAMINER	
HAMA, JOANNE	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/802,996	MEGUID, MICHAEL M.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *9-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This Application, filed March 17, 2004, claims priority to U.S. Provisional Application 60/457,213, filed March 24, 2003.

Claims 1-23 are pending.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-8, in the reply filed on December 22, 2004 is acknowledged.

Claims 9-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 22, 2004.

Claims 1-8, drawn to a surgically modified animal, wherein the animal has a gastrointestinal system that has been surgically modified, wherein the surgical modification reduces the volume of the stomach and reduces the digestive area of the gastrointestinal tract, is under consideration.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 5-7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1-3, 5-7 encompass a human. This is non-statutory matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for non-human mammals having a gastrointestinal system, wherein surgery reduced the volume and digestive area of the gastrointestinal tract and results in permanent reduction of preoperative weight, does not reasonably provide enablement for non-mammalian animals, any transgenic, genetically-modified, or clone animals having a gastrointestinal system, wherein surgery reduced the volume and digestive area of the gastrointestinal tract and results in permanent reduction of preoperative weight. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single,

simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The instantly claimed invention is to an animal having a gastrointestinal system, wherein surgery reduced the volume and digestive area of the gastrointestinal tract and results in permanent reduction of preoperative weight.

The claimed invention encompasses any animal having surgically-mediated gastrointestinal reduction. The art at the time of filing does not teach how to perform a surgical modification wherein the volume of the stomach is reduced and the gastrointestinal tract area is reduced in all animals. For example, the art does not teach that the surgical modification was performed in insects, birds, fish, reptiles, and amphibians. With regards to the anatomy of the stomach, the art teaches that insects do not have stomachs, thus a skilled artisan would not know how to perform reductive surgery in insects. With regards to the enablement of gastrointestinal survival surgery, no teachings in the art that teach survival surgery in birds, fish, reptiles, amphibians. With regards to enablement of survival surgery for mammals that undergo gastrointestinal surgery, the art teaches survival surgery on rats and humans. A skilled

artisan would need to be taught what was performed on any animal, in order to be enabled for the full scope of any animal. It is unclear what steps would need to be taken for anesthesia, what steps were performed during the surgery and what steps a skilled artisan would need to carry out to ensure survival of the animal. These parameters would have to be empirically determined. In addition to these parameters, a skilled artisan would also need to consider other parameters which may affect the survival of the animal after surgery. One consideration is the state of the health of the animal prior to surgery. The focus of the application is on obese animals. Thus, a skilled artisan would need to consider what additional health risks obese animals would have to overcome in order to survive surgery. For example, a review by Pasulka et al. (1986, Annals of Internal Medicine, 104: 540-546) teaches that there are several issues taken into consideration when obese human patients undergo surgery. These include pulmonary issues (Pasulka, et al., page 541-542), circulatory issues (Pasulka, et al., page 542-543), thromboembolic disease (Pasulka, et al., page 543), and wound complications (Pasulka, et al., page 543). In addition to this, at least for humans, life style habits such as diet and smoking can also be factors taken into consideration as risk factors for survival (Pasulka, et al., page 545, see Conclusions). Thus, unless there is reduction to practice, a skilled artisan would not know what steps one would need to obtain any animal surviving from surgery. The specification as filed does not teach how to overcome these surgical issues and thus do not enable a skilled artisan to obtain the broadly claimed invention.

The claimed invention encompass genetically modified non-human mammals. These encompass four main scenarios. (For purposes of analysis, while "genetically modified" non-human mammal encompasses non-human mammal comprising mutations that occur naturally, it should be noted that the "genetically modified" non-human mammals discussed below are ones that have "seen the hand of man.") First, the mouse could be a transgenic non-human mammal, wherein the transgene was introduced into the nucleus of a fertilized egg. Second, the non-human mammal could be a wild type mammal, comprised of cells that were transfected *in vivo* with a DNA expression construct (e.g. gene therapy). Third, the non-human mammal could be a wild type mammal, comprised of cells in a cell culture dish that were transfected with the construct and the cells were then injected into the non-human mammal. Fourth, the non-human mammal could be a non-human knockout mammal. While the claimed invention encompasses these four situations, the specification does not teach that any of these non-human mammals were made.

The claimed invention encompasses transgenic animals. The art at the time of filing teaches that making transgenic animals is unpredictable. Mullins and Mullins (1996, J. Clin. Invest., 97: 1557-1560) teach that making transgenic mammals by nuclear injection was unpredictable. While Mullins and Mullins teach unpredictability for mammals, their argument applies to all transgenic animals. One of the examples of why making transgenic mice was unpredictable was because position effects may affect the expression of the transgene. One problem of unpredictability in generating a transgenic animal stems from the fact that some transgenes integrate in the genome at

places that affect its expression. In some cases, the transgene could insert in the genome and be silenced. In other cases, the transgene could be positioned near an enhancer and be expressed embryonically and then shut off after the developmental stage has been passed. The upshot of this unpredictability is that a skilled artisan would never know when or if one would ever generate a transgenic animal, unless one were actually created. Further, in the case of position effects, a skilled artisan would not know what transgenic animal was generated unless it was characterized. Nothing in the specification teaches how to eliminate the issue of unpredictability, such that one could reliably obtain transgenic animals. For this reason, the specification does not enable a skilled artisan to make any transgenic animal claimed in the instant invention.

The art also teaches that making transgenic animals are unpredictable because a skilled artisan cannot predict that overexpression of a transgene would produce an animal with an expected phenotype. For example, Hammer, et al. (1990, Cell 63:1099-1112) demonstrated that transgenic mice that overexpressed human HLA-B27 and human β2-microglobulin (hβ2m) did not develop the human disease, spondyloarthropathies, whereas a rat that overexpressed human HLA-B27 and human β2-microglobulin (hβ2m) did exhibit spondyloarthropathies (page 1099, second column, second paragraph). The specification as filed does not teach a skilled artisan how to overcome this issue of unpredictability. For this reason, the specification does not enable a skilled artisan to make any transgenic animal claimed in the instant invention.

It is noted that the art teaches several knockout mice and transgenic non-human mammalian models of obesity that were known at the time of filing. However, the

claims as they were written, are broad for any transgenic or genetically modified non-human mammalian model, and thus encompass non-human mammalian models of disease which have nothing to do with weight management (e.g. an Alzheimer's disease mouse model). The specification, as filed, does not teach a skilled artisan how to select candidate non-human mammals in which to perform weight reduction surgery.

With regards to the second non-human mammal, wherein the non-human mammal was injected with a non-viral DNA construct that could express in eukaryotic cells, the specification does not teach a skilled artisan how to make a non-viral DNA construct that could be expressed in eukaryotic cells, nor does the specification teach how to administer such construct. The art teaches several ways that non-viral DNA eukaryotic vectors could be introduced into cells. For example, Wolff et al. teach that some methods of directly introducing non-viral DNA vectors into the animal include non-viral DNA encapsulated in liposomes, Non-viral DNA entrapped in proteoliposomes containing viral envelope receptor proteins, calcium phosphate-coprecipitated DNA, and DNA coupled to polylysine-glycoprotein carrier complex (Wolff, et al., 1990, Science, 247: 1465-1468; page 1465, 1st col., 1st parag., lines 11-18). Wolff et al. teach that non-viral DNA vectors can also be directly injected into muscle. However, the non-viral DNA vector, depending on its route of administration, only localizes to certain tissues or organs. As a result, the vector is not readily distributed throughout the body. For example, Wolff et al. show that the non-viral DNA is localized to the muscle at the site of injection (Wolff, et al., page 1465, 3rd col., 2nd parag.) Nicolau et al. demonstrated that non-viral DNA suspended in liposomes are localized to the liver and the spleen

(Nicolau, et al., 1983, PNAS, USA, 80: 1068-1072; page 1068, 1st col., 1st parag.). Another problem associated with using non-viral DNA vectors is that they suffer from inefficient gene transfer. In addition to this, expression from these non-viral vectors is transient (Somia and Verma, 2000, Nature Reviews, 1:91-99; page 91, 1st col., 2nd parag., lines 2-8)). While it may be that the instant invention is to expressing an exogenous gene in the liver or muscle, and the time of expression required to use the instant invention transient, the specification does not teach that these are the embodiments which are used to practice the invention. The instant invention involves permanent weight loss. This means that expression from a DNA vector needs to be during the duration of the non-human mammal's life span. This means that a skilled artisan would need to determine whether or not the means of introducing a non-viral DNA expression vector is sufficient for the lifetime of the animal and whether the transgene is expressed at detectable levels. To determine these parameters require undue experimentation. In addition to these parameters, a skilled artisan needs to also consider the fact that gene transfer from non-viral vectors is unpredictable. In other words, it may not even be a salient system to use for gene expression. For reasons of unpredictability and undue experimentation, the specification has not enabled a skilled artisan to reliably obtain mice injected with a non-viral transgene construct.

With regards using a viral vector as a vehicle to deliver an exogenous gene, the art teaches that viral vectors as a vehicle is unpredictable. These issues of unpredictability include immune responses to the transgene product, the dose of virus administered, the promoter chosen to drive expression of the recombinant gene, the

innate immune mechanisms and direct cytotoxcity cause by expression of viral genes. For these reasons, the use of a viral vector is determined empirically. However, the specification as filed does not provide sufficient guidance, working examples, and evidence as to how an artisan of skill would have made and used the claimed invention commensurate with the scope of the claims without undue experimentation.

With regards to the third non-human mammal, wherein the wild type non-human mammal is comprised of cells that were transfected in a culture dish and then injected into the non-human mammal, the art teaches that cell and organ transplantation is unpredictable. With regards to a xenogeneic or allogeneic transplant, one major problem associated with these transplants is loss or rejection of the cell. The loss or rejection stems from an immune response to the foreign cell (Platt, 1998, Nature, 392 supplement: 11-17; page 11, 2nd col. under "The barriers to xenotransplantation"). While one might use drugs to immunosuppress a host, the specification does not teach what those drugs may be nor does the specification teach how to administer such drugs (which drugs, how much, route of delivery, for what duration of time). In addition to this, a skilled artisan would need to know how to prevent infection of the host organism, while the host's immune system is suppressed (Platt, page 14, Box 1, 1st parag.). One may suggest that syngeneic cells could be used to circumvent the problem with cell rejection. Certainly, this is a possibility as Gage teaches that syngeneic cells need not integrate into a homotypic region (Gage, 1998, Nature, 392 supplement, pages 18-24; page 18, 2nd col., 1st parag. under "Function of cells as implants"). However, if long-term survival is required, success of the graft appears to depend on the cell type, the

site of implantation, and type or class of promoter (Gage, page 19, 1st col., lines 2-5). Alternatively, if in the cases that require a cell to integrate into a homotypic region and perform specific physiological roles, a skilled artisan would need to know the phenotype of the cell and the spatial location critical to its utility (e.g. a retinal cell transplant or a skin graft) (Gage, page 19, 1st col., 2nd parag. to 2nd col., 2nd parag.). In addition to selecting a cell, a skilled artisan would need to remind oneself that the transplanted cell would be comprised of a DNA expression vector. The art teaches that sometimes following transplantation, a cell comprised of a transgene may alter its level of transgene expression. For example, Fisher teaches that a neuronal cell line, RN33B, show loss of β-gal labeling in cells grafted in the CNS. The change in gene expression does not appear to be because the skilled artisan used a retrovirus. Gene expression is also compromised in cells wherein adenovirus or herpes virus vectors were used (Fisher, 1997, Neurobiology of Disease, 4: 1-22; page 15, 2nd col., 2nd parag. under "In vivo considerations of genetically modified cells," lines 1-13). Thus, for reasons described above, a xenogenic or allogeneic transplant of faces the problem of host rejection. The methods involved to reduce the chance of rejection would need to be empirically determined. Coupled with this, to reduce rejection may involve methods of reducing infection in the host. This, too, would need to be empirically determined. In the case of syngeneic cells, a skilled artisan would need to be taught what kind of cells would need to be isolated, how to isolate said cells, and how to culture said cells. This would need to be empirically determined. Finally, whether a transgene construct can be reliably expressed would also need to be considered. Thus, for the reasons described

above with regard to cell transplantation, the specification as filed does not provide sufficient guidance, working examples and evidence as to how an artisan of skill would have made and used the claimed invention commensurate with the scope of the claims without undue experimentation.

With regards to the fourth type of non-transgenic non-human mammal, the art teaches that the only transgenic non-human mammalian animals that can be generated by using ES cells are mouse, pig, and rabbit. According to Murray, et al. (1999, *Transgenic Animals in Agriculture*, CAB International: Oxon, pages 58-61), the "isolation of ES cells has not been accomplished unequivocally in other species, including in domestic livestock (page 59, lines 3-4)." It is possible that putative ES cells have been isolated in other animals aside from the mouse. These include sheep, hamster, pig, cattle, mink, rabbit, rat, monkey and goat. However, in many cases the data characterizing them do not provide the most convincing data (page 59, lines 10-17). Part of the discrepancy stemmed from the fact that scientists were relying on morphological comparisons of mouse ES cells to define what other animals' ES cells should look like. Some scientists added a second level of stringency, identifying ES cells by the fact that they differentiate *in vitro*. However, the best level of stringency that identifies an ES cells is that the cells can differentiate *in vivo* (page 60, second paragraph). In the case where chimeric offspring have been obtained after injection of putative ES cells into blastocysts, the species include mouse, pig, and rabbit (page 59, lines 18-22). The art teaches that making transgenic animals via ES cells is limited to these animals. The specification does not teach how to obtain other mammalian ES

cells. For this reason, a skilled artisan is not enabled for other transgenic mammals made from ES cells.

The art at the time of filing teaches that numerous factors influence the probability of producing an animal by cloning. In particular, the species of the animal contributes most to the unpredictability. Westhusin et al. (2001, Theriogenology, 55: 35-49) review the state of the art of cloning. They state that, "Without a doubt, one of the major factors influencing the probability of cloning a specific animal is species. While the basic approach involving nuclear transfer may be similar, the specific materials and methods utilized for cloning one species of animal do not automatically apply across different species." (see p. 36, 4th paragraph). Westhusin et al. further state that the factors to consider when cloning animals by nuclear transfer include acquisition of mature ova, enucleation of mature ova, nuclear transfer into the enucleated ova, activation of the newly formed embryo, culturing the embryo *in vitro* and transferring the embryo into a surrogate mother. Furthermore, these techniques and the efficacy of these techniques will vary from species to species (see p. 36-37, bridging paragraph).

Westhusin et al. discuss the state of the art of cloning of cattle, sheep, goat, mice and pigs in detail (see pp. 37-39) and particularly state that the production of cloned animals by somatic cell nuclear transfer has only been reported in the species described above, although there continue to be ongoing experiments in other species of animals (see p. 39, 3rd paragraph). Westhusin et al. further discuss other variables that can affect cloning efficiency, such as the type of donor cells used and genetic modifications (see pp. 40-45).

The specification, as filed, does not teach that any cloned animals were made. Based on the teachings of Westhusin et al., a skilled artisan would need to be taught what species of animal was cloned, the type of donor cells used in the cloning, and the genetic modifications in the donor cell, in order to obtain the claimed invention. However, none of these parameters were taught in the specification and thus do not enable a skilled artisan to produce a cloned animal comprised of a gastrointestinal system, wherein surgery reduced the volume and digestive area of the gastrointestinal tract.

Westhusin *et al.* teach the unpredictable state of the art of nuclear transfer with regard to the unpredictable factors such as species difference, donor cells and genetic modifications. As the specification fails to provide any guidance or teaching for the production of all species of cloned animals, one of skill would not be able to rely upon the state of the nuclear transfer art for an attempt to produce such animals. For this reason, the specification, as filed, does not teach a skilled artisan how to make a clone animal comprised of a gastrointestinal system, wherein surgery reduced the volume and digestive area of the gastrointestinal tract.

For the reasons described above, the specification does not enable a skilled artisan to make any animal comprising a gastrointestinal system wherein surgery reduced the volume and digestive area of the gastointestinal tract, other than in wild type rats and Zucker rats. The specification as filed does not enable a skilled artisan to make the animals of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 uses the word "substantially" to describe "normal (line 4)" and "permanent (line 8)." However, "substantially" is a relative term and depends on the perspective of the skilled artisan.

Claim 1 uses the word "normal (line 4)." However, "normal" is a relative term and no parameters have been provided by the specification teaching what encompasses a "normal" gastrointestinal system.

Claim 1 uses the phrase, "said surgical modification (claim 5)." However, there is no antecedent basis for "surgical modification."

Claim 1 uses the phrase, "said gastrointestinal tract (line 6)." However, there is no antecedent basis for "tract."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 5, 7, 8 are rejected under 35 U.S.C. 102(a) as being anticipated by Xu, et al. (2002, Journal of Surgical Research, 107: 56-63).

The instant invention is to a surgically modified animal comprising a gastrointestinal system that has been surgically modified, wherein the surgical modification reduces the volume of the stomach and reduces the digestive area of the gastrointestinal tract, and wherein the surgically modified animal exhibits reduction of preoperative weight and reduction in preoperative endogenous ghrelin production.

Xu et al. anticipate the claimed invention because they teach that obese Zucker rats were surgically modified with a gastric bypass (GB) with a Roux-en-Y model. Rat gastric fundus was closed using a double-row titanium staple line, thereby creating a 20% pouch. A gastrojejunostomy was then carried out as the jejunum was sewn on the anterior surface of the gastric fundus. A set of rats that were mock-treated for surgery, served as a control for the effects of surgery on the rats (Xu et al., page 57, 2nd col., parag. under "Gastric bypass with Roux-en-Y model"). Xu et al. teach that following surgery, the GB rats ate less, had lower body weights, lower blood glucose and serum insulin concentration, lower free fatty acid and triglyceride concentrations, and lower retroperitoneal and epididymal fat weights than the mock-treated rats (Xu et al., pages 59-61). While Xu et al., do not specifically teach that ghrelin levels are reduced in post-operative obese Zucker rats, the surgically altered animals in the instant invention have been anticipated for reasons of inherency. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or

substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

For this reason, Xu et al. anticipate claims 1, 2, 4, 5, 7, 8.

Claims 1, 2, 4, 5, 7, 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Young et al. (1984, The American Journal of Clinical Nutrition, 40: 293-302).

Young et al. teach that young Zucker rats underwent stomach reduction via stapling of the stomach and then underwent Roux-en-Y reconstruction (Young, 294, 1st col., first paragraph under "Methods"). Young et al. teach these rats ate less than control animals which were treated with no staples, but underwent Roux-en-Y, or laparotomy treated animals (Young, et al., page 299, 1st col., 2nd parag.). Young et al., teach that the morphological pathology observed in the stapled animals were mild. However, they do point out that additional studies need to be carried out to determine the long-term effects of stomach reduction and Roux-en-Y reconstruction on other animals (Young, et al., page 301, 1st col., 2nd parag.). While Young et al., do not specifically teach that ghrelin levels are reduced in post-operative rats, the surgically

altered animals in the instant invention have been anticipated for reasons of inherency. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

For this reason, Young et al. anticipate claims 1, 2, 4, 5, 7, 8.

(Examiner's note: "genetically modified" non-human mammal encompasses mammals comprised of a naturally occurring mutation, see Enablement above.)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5, 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benedetti, et al (2000, Journal of the American College of Nutrition, 19: 270-274) in view of Inui (2000, Pharmacological Review, 52: 35-61).

Benedetti et al. teach that bioliopancreatic bypass with a long Roux-en-Y reconstruction was performed on obese patients. Benedetti et al. teach that unlike classic ileal bypass procedure, the present procedure had the advantages of 1) selective malabsorption of fat, 2) an intact enterohepatic bile salt circulation, and 3) the absence of a long excluded intestinal loop (Benedetti, et al., page 271, Surgical procedure). Benedetti et al. teach that 30 months following surgery, patients, despite high caloric intake, had lost weight. Benedetti et al. also teach that insulin resistance had reversed in patients following surgery, and that glucose and insulin levels were within normal range (Benedetti, et al., page 273, 2nd col,, top). Benedetti et al. teach that there were no long-term side effects with the procedure in the patients (Benedetti, et al., page 274, 1st col., 1st parag.).

Inui provides an overview of non-human, genetically modified mammalian models used in understanding body weight regulation. Inui teaches that transgenic animals have provided ways to modify the complex pathways involved in regulating body weight and to more easily assess the role of individual components in these pathways. Once transgenic animals models are created, they are useful in assessing the efficacy or determining the mode of action of new therapeutic agents (Inui, page 54, 2nd col, 2nd parag.).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use a non-genetically modified non-human obese mammal and a genetically modified non-human mammalian models of obesity, in the surgical method taught by Benedetti et al.

One having ordinary skill in the art would have been motivated to use these non-genetically modified non-human obese mammal and a genetically modified non-human mammalian models of obesity, in order to obtain non-genetically modified non-human obese mammal and a genetically modified non-human mammalian models of obesity that lose weight and can be used to monitor biological effects that occur during weight loss.

There would have been a reasonable expectation of success given Benedetti et al. demonstrating a feasible and safe technique for restricting food intake and malabsorption and Inui teaching that genetically modified non-human mammal models of obesity can be used to assess efficacy of therapeutic agent or to determine the mode of action of potential new agents.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-

272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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JH

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